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19 May 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: ANTISENSE MODULATION OF VEGF CO-REGULATED CHEMOKINE-1 EXPRESSION

(57) Abstract: Antisense compounds, compositions, and methods are provided for modulating the expression of VEGF Co-regulated chemokine-1 (VCC-1). The compositions comprise antisense compounds, particularly antisense oligonucleotides, targeted to nucleic acids encoding VCC-1. Methods of using these compounds for modulation of VCC-1 expression and for treatment of diseases associated with expression of VCC-1 are provided.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/25891

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : C12Q 1/68; A01N 43/04; C07H 21/04; A61K 31/07
US CL : 435/6, 91.1, 325, 375; 536/23.1, 24.3. 24.33, 24.5; 514/44
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 435/6, 91.1, 325, 375; 536/23.1, 24.3. 24.33, 24.5; 514/44

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KOCH et al. Interleukin-8 as a macrophage-derived mediator of angiogenesis. Science. 11 December 1992 Vol. 258, pages 1798-1801, see IL-8 antisense oligonucleotide in Figure 2a at page 1799.	1-14
X	MIYAMOTO et al. Effect of interluekin-8 on production of tumor-associated substnaces and autocrine grwoth of human liver and pancreatic cancer cells. Cancer Immunology Immunotherapy. 1998, Vol. 47, pages 47-57, see IL-8 antisense oligonucleotides at page 48, first column, last paragraph.	1-14
X	SCHADENDORF et al. IL-8 produced by human malignant melanoma cells in vitro is an essential autocrine growth factor. Journal of Immunology. 01 September 1999, Vol. 151, No. 5, pages 2667-2675, see IL-8 antisense oligonucleotides at Table 1.	1-14
X,E	US 2004/0043948 A1 (BAKER et al) 04 March 2004 (04.03.2004), see Table 1.	1-14

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

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21 February 2005 (21.02.2005)

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INTERNATIONAL SEARCH REPORT

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BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

Groups 1-1099. Claims 1-14, drawn to antisense compounds encoding VCC-1, comprising SEQ ID NOs: 1-1099, respectively.

Groups 1100-2198. Claims 15-23, drawn to a method of inhibiting the expression of VCC-1, comprising the administration of an antisense compound encoding VCC-1, comprising SEQ ID NOs: 1-1099.

As outlined above, this international searching authority has found 2198 inventions claimed in the International Application covered by the claims indicated: Claims 1-14 and Claims 15-23, which specifically claim sequences listed as SEQ ID Nos.1-1099, which are intended to modulate the function and/or expression of VCC-1.

This international searching authority considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below:

The inventions listed as Groups 1-16 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

According to the guidelines in Section (f)(i)(a) of Annex B of the PCT Administrative Instructions, the special technical feature as defined by PCT Rule 13.2 shall be considered to be met when all the alternatives of a Markus group are of similar nature. For chemical alternatives, such as the claimed antisense sequences, the Markush group shall be regarded as being of similar nature when
(A) all alternatives have a common property or activity and
(B)(1) a common structure is present, i.e., a significant structure is shared by all of the alternatives or
(B)(2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to an art recognized class of compounds in the art to which the invention pertains.

The instant antisense sequences are considered to be each separate inventions for the following reasons:

The sequences do not meet the criteria of (A), common property or activity or (B)(2), art recognized class of compounds. Although the sequence target and modulate expression of the same gene, each antisense sequence behaves in a different way in the context of the claimed invention. Each sequence targets a different and specific region of liver EDG1 and each sequence modifies (either increases or decreases) the expression of the gene to varying degrees (per Applicants' Table I in the specification). Each member of the class cannot be substituted, one for the other, with the expectation that the same intended result would be achieved.

Further, although the sequence target the same gene, the sequences do not meet the criteria of (B)(1), as they do not share, one with another, a common core structure. Accordingly, unity of invention between the antisense sequences is lacking and each antisense sequence claimed is considered to constitute a special technical feature.

Applicants will obtain a search of the first sequence listed in the first invention. For every other sequence applicants wish to have searched, applicants need to elect the sequence and pay an additional fee.

Continuation of B. FIELDS SEARCHED Item 3:

INTERNATIONAL SEARCH REPORT

PCT/US03/25891

CaPlus, EmBase, CancerLit, Medline, WEST
search terms: vascular endothelial growth factor (VEGF) and co-regulated chemokine, VCC-1, CXC chemokine, interleukin 8, IL-8, antisense, and ribozyme

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US03/25891

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-14; SEQ ID NO:1

Remark on Protest
☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.